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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,740	12/01/2006	Bernard Freiss	3493-0179PUS1	5296

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EXAMINER	
LAU, JONATHAN S	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/594,740	FREISS ET AL.	
	Examiner	Art Unit	
	Jonathan S. Lau	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-21 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-21 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is responsive to Applicant's Amendment and Remarks, filed 30 Dec 2009, in which claims 11 and 17 are amended to change the scope and breadth of the claim.

This application is the national stage entry of PCT/FR05/00739, filed 29 Mar 2005; and claims benefit of foreign priority document FRANCE 0403450, filed 01 Apr 2004, and foreign priority document FRANCE 0411201, filed 21 Oct 2004; currently English language translations of these foreign priority document have not been filed.

Claims 11-21 and 26 are pending and examined on the merits herein.

Rejections Withdrawn

Applicant's Amendment, filed 30 Dec 2009, with respect to claims 11-21 and 26 rejected under 35 U.S.C. 103(a) as being unpatentable over Van Hees et al. 2002 (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, p271-274, provided by Applicant on IDS filed 29 Sep 2006) as evidenced by Van Hees et al. 1999 (Pharmaceutical Research, 1999, 16, p1864-1870, provided by Applicant on IDS filed 29 Sep 2006) and in view of Junco et al. (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, 69-73, of record) has been fully considered and is persuasive, as amended claim 11 recites the active step c. of depressurizing and recovering the active substance/host molecule complex. Although now moot in view of

the amended claim, to clarify the record the definition of "recovering" within the chemical arts is interpreted such that it is not limited to separation which is one definition within the chemical arts, but rather the ordinary definition of "recovering" is encompassed and included by the term within the context of the chemical arts.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 30 Dec 2009, with respect to claims 11-22 and 26 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 and 13 of copending Application No. 10/554,058 in view of Van Hees et al. 2002 (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, p271-274, provided by Applicant on IDS filed 29 Sep 2006) has been fully considered and is persuasive, as amended claim 11 recites the active step c. of depressurizing and recovering the active substance/host molecule complex.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 30 Dec 2009, with respect to claims 11-22 and 26 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 and 13 of copending Application No. 10/554,058 in view of Van Hees et al. 2002 (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, p271-274, provided by Applicant on IDS filed 29 Sep 2006) has been fully considered and is persuasive, as amended claim 11 recites the

active step c. of depressurizing and recovering the active substance/host molecule complex followed by step d. of adding to and mixing with the active substance/host molecule molecular complex an agent for interaction with the complex.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 30 Dec 2009, with respect to claims 11-21 and 26 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 7,390,411, now issued from copending Application No. 10/492,346, in view of Van Hees et al. 2002 (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, p271-274, provided by Applicant on IDS filed 29 Sep 2006) has been fully considered and is persuasive, as amended claim 11 recites the active step c. of depressurizing and recovering the active substance/host molecule complex followed by step d. of adding to and mixing with the active substance/host molecule molecular complex an agent for interaction with the complex.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 30 Dec 2009, with respect to claims 11-21 and 26 rejected under 35 U.S.C. 112, first paragraph, as not being enabled for the full scope of the claim has been fully considered and is persuasive, as amended claim 11 recites the active step d. of adding to and mixing with the active substance/host molecule molecular complex an agent for interaction with the complex in a semi-solid medium.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 30 Dec 2009, with respect to claims 11-21 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite has been fully considered and is persuasive, as amended claim 11 recites an aqueous soluble inclusion compound and amended claim 17 does not recite "anilide derivatives" at line 2 and "epipodophyllotoxin derivatives" at lines 2-3.

This rejection has been **withdrawn**.

The following are new grounds of rejection necessitated by Applicant's Amendment, filed 30 Dec 2009, in which claims 11 and 17 are amended to change the scope and breadth of the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11-13, 15-21 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Junco et al. (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, 69-73, of record) in view of Majid et al. (US Patent 5,070,081, issued 3 Dec 1991, cited in PTO-892).

Junco et al. teaches the complexation of a pharmaceutically active substance naproxen with β-cyclodextrin using super-critical CO_2 (page 69, abstract). Junco et al. teaches the addition of a small amount of co-solvent to a supercritical fluid can have dramatic effects on its solvent power (page 70, left column, lines 4-6), said co-solvent corresponding to the instant claimed diffusion agent. Junco et al. specifically teaches the use of co-solvents ethyl acetate, acetone, methanol, ethanol, 1-propanol and 2-propanol (page 70, left column, lines 6-11). Junco et al. teaches the use of ethanol added continuously in the amount of 4% by weight (page 70, right column, line 17). Junco et al. teaches embodiments wherein the dense pressurized fluid is at a pressure of 125 bar, or 12.5 MPa, at 65 °C (page 70, right column, paragraph 3) or 160 bar, or 16.0 MPa, at 62 °C with stirring (page 70, right column, paragraph 4). Junco et al. teaches that at the end of the complexation the system is depressurized by venting (page 70, right column, paragraph 4).

Junco et al. does not specifically teach the active step d. of adding to and mixing with the active substance/host molecule molecular complex an agent for interaction with the complex in a semi-solid medium (instant claim 11).

Majid et al. teaches it is routine in the prior art in the field of inclusion complexes of cyclodextrins to perform a step of pelletization or agglomeration after complex formation, from which the invention of Majid et al. forms an improvement (column 2, lines 5-20). Majid et al. teaches it is advantageous for water to be present during the formation of the agglomerates (column 2, lines 20-35), providing guidance for selecting the mixing performed in a semi-solid medium. Majid et al. teaches the mixing with a Spex mixer in a glass jar sealed tightly (column 3, lines 30-35), implicitly under atmospheric pressure. Majid et al. teaches the step of recovering the agglomerates of the inclusion complex (column 2, lines 35-40). Majid et al. teaches within the context of the invention of Majid et al. that any final wet pelletization procedure may be used to form the final agglomerates (column 2, lines 45-55) and that added water has been found necessary for agglomeration (column 2, lines 55-60). The water taught by Majid et al. is interpreted as the agent for interaction with the complex. It is well known that water is an amphoteric substance, in that it can react as an acid or a base.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine Junco et al. in view of Majid et al. Both Junco et al. and Majid et al. are drawn to pharmaceutical forms of inclusion complexes of cyclodextrins. One of ordinary skill in the art at the time of the invention would be motivated to combine Junco et al. in view of Majid et al. because Majid et al. teaches it is routine in the prior art in the field of inclusion complexes of cyclodextrins to perform a step of pelletization or agglomeration after complex formation. One of ordinary skill in the art would have a reasonable expectation of success in combining the formation of the complex taught by

Junco et al. with the agglomerization taught by Majid et al. because Majid et al. teaches those steps being separate are routine in the art and within the context of the invention of Majid et al. that any final wet pelletization procedure may be used to form the final agglomerates.

Response to Applicant's Remarks:

Applicant's Remarks, filed 30 Dec 2009, have been fully considered and found not to be persuasive.

Applicant remarks that the instant invention is drawn to a two-step process for the preparation of an aqueous soluble inclusion compound. However, instant invention as recited by the language in the claims is interpreted to encompass the method made obvious by Junco et al. in view of Majid et al. in which Junco et al. teaches the complex formation (instant steps a-c) combined with Majid et al teaching a step of agglomeration or wet pelletization (instant steps d-e) to give an agglomerated or pelletized form of aqueous soluble inclusion compound.

Claims 11-21 and 26 rejected under 35 U.S.C. 103(a) as being unpatentable over Junco et al. (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, 69-73, of record) in view of Majid et al. (US Patent 5,070,081, issued 3 Dec 1991, cited in PTO-892) and Lieberman et al. (Pharmaceutical dosage forms-- disperse systems, 1998, Marcel Dekker, Inc., 2nd ed., p1-46, cited in PTO-892).

Junco et al. teaches the complexation of a pharmaceutically active substance naproxen with β-cyclodextrin using super-critical CO_2 (page 69, abstract). Junco et al.

teaches the addition of a small amount of co-solvent to a supercritical fluid can have dramatic effects on its solvent power (page 70, left column, lines 4-6), said co-solvent corresponding to the instant claimed diffusion agent. Junco et al. specifically teaches the use of co-solvents ethyl acetate, acetone, methanol, ethanol, 1-propanol and 2-propanol (page 70, left column, lines 6-11). Junco et al. teaches the use of ethanol added continuously in the amount of 4% by weight (page 70, right column, line 17). Junco et al. teaches embodiments wherein the dense pressurized fluid is at a pressure of 125 bar, or 12.5 MPa, at 65 °C (page 70, right column, paragraph 3) or 160 bar, or 16.0 MPa, at 62 °C with stirring (page 70, right column, paragraph 4). Junco et al. teaches that at the end of the complexation the system is depressurized by venting (page 70, right column, paragraph 4).

Junco et al. does not specifically teach the active step d. of adding to and mixing with the active substance/host molecule molecular complex an agent for interaction with the complex in a semi-solid medium (instant claim 11).

Majid et al. teaches it is routine in the prior art in the field of inclusion complexes of cyclodextrins to perform a step of pelletization or agglomeration after complex formation, from which the invention of Majid et al. forms an improvement (column 2, lines 5-20). Majid et al. teaches it is advantageous for residual water to be present during the formation of the agglomerates (column 2, lines 20-35), providing guidance for selecting the mixing performed in a semi-solid medium. Majid et al. teaches within the context of the invention of Majid et al. that any final wet pelletization procedure may be used to form the final agglomerates (column 2, lines 45-55).

Lieberman et al., drawn to the field of pharmaceutical suspensions including solid-liquid and solid-solid suspensions (page 2, paragraphs 3 and table 1), teaches flocculated suspensions made by agglomeration (page 18, paragraph 2-4). Lieberman et al. teaches it is routine in the art to formulate physically stable pharmaceutical suspensions using wetting agents, flocculating agents, stabilizers and preservatives (spanning pages 26-27, section V. FORMULARION OF SUSPENSIONS). Lieberman et al. teaches stabilizers include disodium edetate (page 30, paragraph 2), or ethylenediaminetetraacetic acid, a compound that contains both amine and a carboxylic acid moieties, or an amino acid. Lieberman et al. teaches preservatives include carboxylic acids such benzoic acid and sorbic acid (page 31, paragraph 1 and page 32, table 9).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine Junco et al. in view of Majid et al. and Lieberman et al. All of Junco et al., Lieberman et al. and Majid et al. are drawn to the field of pharmaceutical processing specifically in particle formation processes. The term "an agent for interaction with the complex" is defined in the specification as "any organic or inorganic agent which improves the physicochemical properties, in particular the properties of dissolution in an aqueous medium, of the molecular complex by interactions without covalent bonds with the active substance included in the host molecule - or directly with the molecular complex" (instant specification, page 9, lines 20-30). This term is interpreted to encompass the wetting agents, flocculating agents, stabilizers and preservatives taught by Lieberman et al. to be mixed during the formulation of a

pharmaceutical suspension. The instant method as claimed is interpreted as encompassing making the inclusion complex of cyclodextrin taught by Junco et al. (steps a-c) followed by formulation by pelletization or agglomeration taught by Majid et al. and Lieberman et al. (steps d-e) to prepare an aqueous soluble inclusion compound as part of a pharmaceutical suspension. One of ordinary skill in the art would have been motivated to combine Junco et al. in view of Majid et al. and Lieberman et al. because Majid et al. teaches it is routine in the prior art in the field of inclusion complexes of cyclodextrins to perform a step of pelletization or agglomeration after complex formation and Lieberman et al. teaches the routine formulation of physically stable pharmaceutical suspensions.

Response to Applicant's Remarks:

Applicant's Remarks, filed 30 Dec 2009, have been fully considered and found not to be persuasive.

With regard to step e., the definition of "recovering" within the chemical arts is interpreted that it is not limited to separation which is one definition within the chemical arts, but rather the ordinary definition of "recovering" is encompassed and included by the term within the context of the chemical arts. The term is interpreted to encompass to recovering the aqueous soluble inclusion compound as part of a pharmaceutical formulation from a pelletization or agglomeration mixer because the term "recovering" is not clearly defined to require separating, isolating or purifying said aqueous soluble inclusion compound.

Conclusion

No claim is found to be allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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